First-in-Human Studies: Global Regulatory and Translational Considerations

Moscone North, Room 135

Wednesday, October 30, 2013, 8:00 AM–11:48 AM

Abstract nos: 122-126

TCT-122

Electrode irrigation alters RF ablation treatment zone geometry and preserves medial and adventitial tissue while maintaining injury to renal nerves

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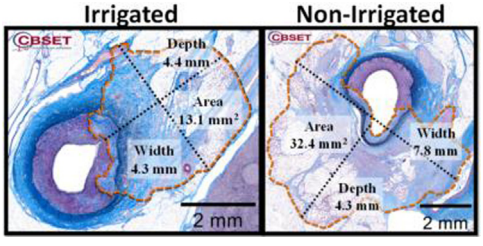
Background: We quantitatively compared lesion geometry and artery and nerve injury with and without irrigation during RF ablation to enable optimization of catheter design and understanding of temperature gradients.
Methods: RF ablations, using spatially discrete electrodes, were conducted in swine using THERMOCOOL® irrigated tip catheter (Biosense Webster, CA) with and without irrigation. Arteries were harvested at 7d and serial sectioned every 300 µm and quantified histomorphometrically (Fig 1).



Results: Surface irrigation lowered affected luminal circumference (irrigated 6.1% vs. non-irrigated 44.6%); media (irrigated 11.7% vs. non-irrigated 35.4%); and EEL circumference (irrigated 18.9% vs. non-irrigated 45.4%). RF ablation effects in the nerve-rich adventitia were less sensitive to irrigation: width (irrigated 3.8mm vs. non-irrigated 4.8mm) and depth (irrigated 5.1mm vs. non-irrigated 3.4mm). Morphologic nerve changes within the ablation zones were comparable with and without irrigation and were considered to be marked and necrotic/degenerative.
Conclusions: Irrigation preserved arterial integrity and reduced linear, circumferential, and radial injury at the luminal surface and within media and adventitia while providing comparable nerve injury. These data were used to develop a computational model of RF energy delivery and injury for further optimization of irrigation and powering protocols.

TCT-123

Preliminary safety and efficacy results from the REALISE trial: REnAL denervatIon by ultraSound transcatheter Emission

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Background: Catheter-based renal denervation has emerged as a method for treating the overactivity of the sympathetic nervous system. The PARADISE system (ReCor Medical, Menlo Park, CA) is a unique therapeutic non-focused ultrasound system designed to perform circumferential renal denervation while preventing damage to the renal artery. The purpose of the REALISE trial is to evaluate the safety and efficacy of the PARADISE system in patients suffering from resistant hypertension.
Methods: The REALISE trial is a 20-patient prospective study conducted by multi-disciplinary teams at two sites in France (Hôpital Pitié-Salpêtrière, Paris; Hôpital Rangueil, Toulouse). Patients suffering from resistant hypertension as defined by the ESH-ESC guidelines (office blood pressure above 140/90 mmHg with a minimum of 3 antihypertensive drugs including a diuretic) were screened and eligibility further confirmed by home and/or ambulatory measurements. Renal denervation was performed bilaterally with the PARADISE system, delivering 2 to 3 ultrasound emissions in each artery. All patients underwent CT-scan or MRI at baseline and follow-up to assess the renal arteries.
Results: Preliminary results indicated that 63% of enrolled and treated patients were under spironolactone therapy. Bilateral denervation was performed by delivering an average of 5.7 ultrasound emissions in each subject (average heating time 3.3 minutes per subject). Sedatives and analgesics were administered during the intervention and the treatment was well tolerated by all patients. Preliminary results at 6 months were comparable to published data on radiofrequency renal denervation with an average reduction in office and ambulatory blood pressure of -21/-9 mmHg and 9/ 4 mmHg, respectively. Systematic imaging of the renal arteries showed no arterial stenosis or arterial damage at follow-up.
Conclusions: Endovascular ultrasound renal denervation appears to be a safe and effective treatment for resistant hypertension. Results on all 20 patients from the REALISE study will be presented at the conference.

TCT-124

A novel appliance for transcatheter mitral cerclage annuloplasty

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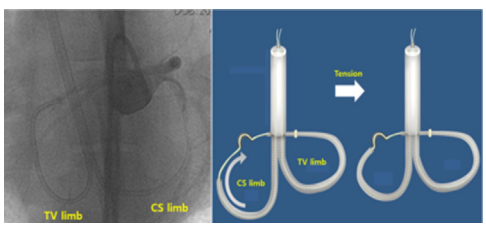
Background: Mitral cerclage annuloplasty is a transcatheter coronary sinus annuloplasty that establishes circumferential tension around the mitral annulus by traversing the basal interventricular septum between the great cardiac vein and the right ventricular outflow tract. We have developed a novel implant to effect annuloplasty while preventing myocardial erosion; avoiding compression of coronary arteries, tricuspid leaflet, AV node; and displaceing the knot fixation to a safe caval location.
Methods: The cerclage appliance is positioned over a 0.018" nylon-coated flexible and radiopaque stainless steel braidwire. It consists of conjoined semirigid coronary sinus and trans-tricuspid limbs (CS, TV, Figure) and is used along with a coronary artery protection arch. X-ray guided cerclage was performed in swine (n=6, 55～80kg) to investigate the device performance.
Results: The cerclage appliance was easily delivered over the cerclage suture and assumed its intended anatomic position along the coronary sinus and across the tricuspid valve. Tension accomplished circumferential mitral annular reduction while the TV limb protected the TV and AV node from direct contact. Neither conduction block nor TV malfunction was observed after two-week survival (n=1).
Conclusions: This novel cerclage appliance addresses potential shortcomings of transcatheter cerclage annuloplasty in a simple-to-deploy device.



TCT-125

Novel Thoracoscopically Assisted Trans-Catheter Ventricular Restoration Therapy: Feasibility and Efficacy in an Anteroseptal Aneurysmal Ovine Model

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Background: Surgical ventricular reconstruction has been used as heart failure treatment in patients with large ventricular aneurysms. Based on a well-established device-based (BioVentrix, San Ramon, CA) surgical technique operation, this study assessed the feasibility of performing minimally invasive thoracoscopically assisted transcatheter ventricular restoration (TCVR) in an anteroseptal ovine infarction model.
Methods: Ventricular aneurysmal model development was achieved by coil-occlusion of the left anterior descending artery. 8 weeks after occlusion, TCVR was performed in five sheep via a 4 cm left thoracotomy. Under endoscopic and fluoroscopic guidance, LV scar was visualized and trans-epicardial puncture was performed advancing a guidewire at the lateral margin of the scar, across a portion of the LV, and through the interventricular septum into the right ventricle. With one end still protruding from the left chest, the guidewire was retrieved with a snare via the right external jugular vein through a percutaneous approach. Then an inner anchor on a tether was inserted over the wire and positioned on the right side of the interventricular septum. The opposite end of the tether protruded through LV anterolateral wall and an outer locking anchor was deployed over the tether on the LV anterior epicardium. Serial pairs of anchors were then approximated to exclude the intervening portion of the

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